Complete Summary

GUIDELINE TITLE

Guidelines on the diagnosis and management of solitary plasmacytoma of bone and solitary extramedullary plasmacytoma.

BIBLIOGRAPHIC SOURCE(S)

Soutar R, Lucraft H, Jackson G, Reece A, Bird J, Low E, Samson D, Guidelines Working Group of the UK Myeloma Forum, British Committee for Standards in Haematology, British Society for Haematology. Guidelines on the diagnosis and management of solitary plasmacytoma of bone and solitary extramedullary plasmacytoma. Br J Haematol 2004 Mar;124(6):717-26. [59 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Solitary plasmacytoma of bone
- Solitary extramedullary plasmacytoma

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Hematology
Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

Not stated

TARGET POPULATION

Patients with solitary bone plasmacytoma (SBP) or solitary extramedullary plasmacytoma (SEP)

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Diagnostic criteria for solitary bone plasmacytoma (SBP)
2. Other Tests
    - Full blood count
    - Biochemical screen including electrolytes and corrected calcium
    - Serum immunoglobulin levels
    - Serum and urine protein electrophoresis and immunofixation
    - Full skeletal survey, including standard X-rays of the skeleton including lateral and anteroposterior cervical, thoracic and lumbar spine, skull, chest, pelvis, humeri and femora
    - Magnetic resonance imaging (MRI) of thoracic and lumbar spine
    - Bone marrow aspirate and trephine
3. Diagnostic criteria for solitary extramedullary plasmacytoma (SEP)
4. Imaging
    - Computed tomography and MRI

Treatment

1. SBP
    - Radical radiotherapy
    - Chemotherapy
    - High dose therapy and autologous haemopoietic stem cell transplantation
    - Monitoring to detect progression to multiple myeloma (MM)
    - Treatment of MM
    - Surgery
2. SEP
    - Radical radiotherapy
    - Surgery
    - Adjuvant chemotherapy

3. Provision of patient information and support

MAJOR OUTCOMES CONSIDERED

- Progression to multiple myeloma (MM)
- Response to treatment
- Survival

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A literature search was performed by a professional librarian using MEDLINE and EMBASE from 1996 to March 2002. A search was made for randomized-controlled trials involving plasmacytoma, papers where plasmacytoma was the major focus of the paper and reviews where plasmacytoma was the major focus.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Ia Evidence obtained from meta-analysis of randomised controlled trials

Ib Evidence obtained from at least one randomised controlled trial

IIa Evidence obtained from at least one well-designed, non-randomised study, including phase II trials and case $\pm$ control studies

IIb Evidence obtained from at least one other type of well-designed, quasi-experimental study (i.e. studies without planned intervention, including observational studies)

III Evidence obtained from well-designed, non-experimental descriptive studies. Evidence obtained from meta-analysis or randomised controlled trials or phase II studies which is published only in abstract form

IV Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The literature was reviewed by the subgroup of the Guidelines Working Group of the UK Myeloma Forum.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Solitary bone plasmacytoma (SBP) and solitary extramedullary plasmacytoma (SEP) are rare diseases and most of the evidence relates to retrospective data from patient series collected over long periods of time. Very few formal clinical trials have been performed. The majority of the recommendations given are therefore based on consensus of expert opinion.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendations

Grade A, evidence level Ia, Ib

Recommendation based on at least one randomised controlled trial of good quality and consistency addressing specific recommendation

Grade B, evidence level IIa, IIb, III

Recommendation based on well-conducted studies but no randomised controlled trials on the topic of recommendation

Grade C, evidence level IV

Evidence from expert committee reports and/or clinical experiences of respected authorities

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Not stated

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not applicable

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence **(I–IV)** and strength of recommendations **(A–C)** are defined at the end of the "Major Recommendations" field.

Solitary Bone Plasmacytoma (SBP)

Diagnosis and Investigation of Solitary Bone Plasmacytoma

Diagnostic criteria

Recommended diagnostic criteria are summarized in the table below, titled "Recommended diagnostic criteria for solitary bone plasmacytoma (SBP) and extramedullary plasmacytoma (SEP)." Based on the data discussed above, the following criteria are recommended:

- Single area of bone destruction due to clonal plasma cells
- Histologically normal marrow aspirate and trephine (<5% plasma cells)
- Normal results on skeletal survey, including radiology of long bones
- No anaemia, hypercalcaemia or renal impairment due to plasma cell dyscrasia
- Absent or low serum or urinary level of monoclonal immunoglobulin (level of >20 g/l suspicious of multiple myeloma (MM))
- No additional lesions on magnetic resonance imaging (MRI) scan of the spine (see below for criteria of involvement)

Pathology review

Solitary bone plasmacytoma is generally diagnosed by biopsy or fine needle aspiration. Percutaneously guided biopsy of the spine is usually possible either by fluoroscopy or computed tomography (CT). As these tumours are rare, pathology review by a histopathologist with a special interest in either bone tumours or lymphoproliferative disorders is strongly recommended.

Further investigations

The following investigations should be performed in all patients:

- Full blood count
- Biochemical screen including electrolytes and corrected calcium
- Serum immunoglobulin levels
- Serum and urine protein electrophoresis and immunofixation

- Full skeletal survey, including standard X-rays of the skeleton including lateral and anteroposterior cervical, thoracic and lumbar spine, skull, chest, pelvis, humeri and femora
- MRI of thoracic and lumbar spine
- Bone marrow aspirate and trephine

Additional investigations may be useful in selected patients, including

- MRI of pelvis, proximal femora and humeri
- Immunophenotyping and molecular assessment of bone marrow plasma cells
- Positron emission tomography (PET) scanning

Treatment of SBP

Radiotherapy

It is recommended that SBP is treated with radical radiotherapy, encompassing the tumour volume shown on magnetic resonance imaging (MRI) with a margin of at least 2 cm and treating to a dose of 40 Gy in 20 fractions (**grade B recommendation, based on level III evidence**).

For SBP >5 cm, a higher dose of up to 50 Gy in 25 fractions should be considered (**grade C recommendation, based on level IV evidence**).

Patients with SBP require careful monitoring to detect progression to MM, possibly 6 weekly for 6 months with extension of clinic appointments thereafter. Assessment of signs and symptoms should be undertaken in conjunction with laboratory investigations (haematology, biochemistry, serum and urine paraprotein estimation) (**grade C recommendation, based on level IV evidence**).

Patients not responding to radiotherapy (see above) should be treated with chemotherapy. A suggested approach is to follow guidelines for the treatment of MM. In younger patients, this would include high dose therapy and autologous haemopoietic stem cell transplantation (**grade C recommendation, based on level IV evidence**).

Patients presenting as SBP but found on MRI to have disease at other sites should be considered as having MM and treated accordingly (**grade B recommendation, based on level II evidence**).

Surgery

Radiotherapy remains the treatment of choice for SBP and surgery is contra-indicated in the absence of structural compromise or neurological compromise (**grade C recommendation, based on level IV evidence**).

Where surgery is required, radiotherapy should also be given and the timing of surgery relative to radiotherapy should be determined for each patient (**grade C recommendation, based on level IV evidence**).

In cases of spinal plasmacytoma, referral for an opinion from an orthopaedic surgeon or neurosurgeon specializing in spinal surgery is advised (**grade C recommendation, based on level IV evidence**).

Reconstruction of the anterior column may be beneficial (**grade C recommendation, based on level IV evidence**).

Adjuvant Chemotherapy

There are insufficient data to recommend adjuvant chemotherapy in SBP.

It may be appropriate to consider adjuvant chemotherapy in patients at higher risk of treatment failure (e.g. those with bulky disease [>5 cm]) (**grade C recommendation, based on level IV evidence**).

Solitary Extramedullary Plasmacytoma (SEP)

Diagnosis and Investigation of SEP

Diagnostic criteria

CT or MRI scanning is required to delineate the extent of the lesion but the role of MRI scanning of other areas in the staging of SEP has not been evaluated. As there is a low risk of progression to MM in these patients and the role of MRI in the staging of SEP has not been studied, we do not consider MRI of the spine to be necessary for the diagnosis of SEP. Recommended diagnostic criteria are shown in table below, titled "Recommended diagnostic criteria for solitary bone plasmacytoma (SBP) and extramedullary plasmacytoma (SEP)."

Pathology review

For most patients the diagnosis can be established by fine needle aspiration or biopsy. As these tumours are rare, and can be confused with non-Hodgkin's lymphoma, pathology review by a histopathologist with a special interest in lymphoproliferative disorders is strongly recommended.

Investigations

As noted above, CT or MRI scanning is required to delineate the extent of the lesion but we do not consider MRI of other areas (see above) to be necessary. Other investigations should be as for SBP (see above).

Treatment of SEP

Radiotherapy

Solitary extramedullary plasmacytoma should be treated by radical radiotherapy encompassing the primary tumour with a margin of at least 2 cm (**grade B recommendation, based on level III evidence**).

The cervical nodes should be included if involved. The first echelon cervical nodes should be included in SEP of Waldeyer's ring (**grade B recommendation, based on level III evidence**).

For SEP up to 5 cm a radiotherapy dose of 40 Gy in 20 fractions is recommended.

For bulky SEP of >5 cm, a higher dose of up to 50 Gy in 25 fractions is recommended (**grade B recommendation, based on level III evidence**).

Surgery

Radiotherapy alone is the treatment of choice for head and neck SEP (**grade B recommendation, based on level III evidence**).

Radical surgery should be avoided in head and neck SEP (**grade C recommendation, based on level IV evidence**).

For SEP at other sites complete surgical removal should be considered if feasible (**grade B recommendation, based on level III evidence**).

Patients with involved surgical margins should receive adjuvant radiotherapy (**grade C recommendation, based on level IV evidence**).

No recommendation for adjuvant radiotherapy can be made for patients who have undergone complete surgical excision with negative margins.

Adjuvant chemotherapy

Adjuvant chemotherapy should be considered in patients with tumours >5 cm and those with high grade tumours (**grade C recommendation, based on level IV evidence**).

Chemotherapy is indicated for patients with refractory and/or relapsed disease. Therapy as for MM is indicated (**grade C recommendation, based on level IV evidence**).

Patient information and support

Provision of appropriate patient information and support forms an important part of the care of patients with SBP and SEP. General principles are the same as those for patients with myeloma. The International Myeloma Foundation (UK) produces a booklet for patients with solitary plasmacytoma.

Table. Recommended Diagnostic Criteria for Solitary Bone Plasmacytoma (SBP) and Extramedullary Plasmacytoma (SEP)

Solitary bone plasmacytoma Single area of bone destruction due to clonal plasma cells

Histologically normal marrow aspirate and trephine
Normal results on skeletal survey, including radiology of long bones
No anaemia, hypercalcaemia or renal impairment due to plasma cell dyscrasia
Absent or low serum or urinary level of monoclonal immunoglobulin
No additional lesions on MRI scan of the spine
Solitary extramedullary plasmacytoma
Single extramedullary mass of clonal plasma cells
Histologically normal marrow aspirate and trephine
Normal results on skeletal survey, including radiology of long bones
No anaemia, hypercalcaemia or renal impairment due to plasma cell dyscrasia
Absent or low serum or urinary level of monoclonal immunoglobulin

Definitions:

Levels of Evidence

Ia Evidence obtained from meta-analysis of randomised controlled trials

Ib Evidence obtained from at least one randomised controlled trial

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IV Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

Grades of Recommendations

Grade A, evidence level Ia, Ib

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Grade B, evidence level IIa, IIb, III

Recommendation based on well-conducted studies but no randomised controlled trials on the topic of recommendation

Grade C, evidence level IV

Evidence from expert committee reports and/or clinical experiences of respected authorities

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for most of the recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Accurate diagnosis and appropriate management of solitary bone plasmacytoma (SBP) and solitary extramedullary plasmacytoma (SEP) to enable, control or cure of disease, prevention of progression to multiple myeloma (MM), and control of pain

POTENTIAL HARMS

Side effects of treatment

CONTRAINDICATIONS

CONTRAINDICATIONS

- Radiotherapy remains the treatment of choice of the primary pathology and surgery is contra-indicated in the absence of structural instability or neurological compromise.
- The relatively new technique of vertebroplasty, which has been used with success in multiple myeloma (MM), has not been reported in solitary plasmacytoma. It is contra-indicated in cases of neurological involvement.

QUALIFYING STATEMENTS

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The advice and information in these guidelines is believed to be true and accurate at the time of going to press. However, the authors, the British Society for Haematology and the publishers do not accept any legal responsibility or liability for any errors or omissions that may have been made.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Soutar R, Lucraft H, Jackson G, Reece A, Bird J, Low E, Samson D, Guidelines Working Group of the UK Myeloma Forum, British Committee for Standards in Haematology, British Society for Haematology. Guidelines on the diagnosis and management of solitary plasmacytoma of bone and solitary extramedullary plasmacytoma. Br J Haematol 2004 Mar;124(6):717-26. [59 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Mar

GUIDELINE DEVELOPER(S)

British Committee for Standards in Haematology - Professional Association

SOURCE(S) OF FUNDING

British Committee for Standards in Haematology

GUIDELINE COMMITTEE

Guidelines Working Group of the UK Myeloma Forum (UKMF)

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Working Group Members: Richard Soutar, Consultant in Haematology and Transfusion Medicine; Helen Lucraft, Consultant Clinical Oncologist; Graham Jackson, Consultant Haematologist; Anthony Reece, Consultant Orthopaedic Surgeon; Jenny Bird, Consultant Haematologist; Eric Low, International Myeloma Foundation UK (patient advocate group); Diana Samson, Chairman UK Myeloma Forum

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the British Committee for Standards in Haematology Web site.

Print copies: Available from Dr Richard Soutar, Department of Haematology, Western Infirmary, Dumbarton Road, Glasgow G11 6NT, UK; E-mail: rls4m@clinmed.gla.ac.uk

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on September 27, 2006. The information was verified by the guideline developer on October 25, 2006.

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